D. Remarks

Reconsideration and allowance in view of the amendments made and comments which follow are respectfully requested.

Claims 1-60 are pending in this application. Claims 1, 12, 20, 31, 39, 50 and 58-60 are being amended.

In the Office Action dated May 1, 2003, claims 1-60 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner stated that applicant has amended independent claims 1, 12, 20, 31, 39, 50, 58, 59 and 60 to include using the method/device for treatment "to prevent or reverse arrhythmias". The applicant has cited the specification to support these new limitations, specifically: 1) page 5, line 5 - "It is a further objective of the invention to provide an apparatus and method for pacing of the heart for sustained periods of time to induce remodeling of gap junctions and ion channels, to sustain an antiarrhythmic effect and alter contractile patterns as well.", 2) page 41, line 13 - relative to the activation-recovery intervals and effective refractory periods at the same sites, the remodeling "provides greater protection at each site from the propagation of premature depolarizations that had occurred previously, in other words, a profound antiarrhythmic effect." 3) page 42, lines 12-15 - "the pacing invention performed is most likely to prevent it (the arrhythmia) from either expressing or

sustaining itself."

The Examiner stated that these passages do not support the new limitation. The Examiner stated that these citations support "to prevent arrhythmias", "to sustain an antiarrythmic effect", "to alter contractile patterns", and "to provide an antiarrhythmic effect", but they do not support "to reverse arrhythmias". The Examiner stated that the phrase "to prevent or reverse arrhythmias" is viewed as new matter, and new matter may not be introduced at this point in the prosecution. The Examiner stated that appropriate correction is required. Without conceding the correctness of the Examiner's decision, but solely to advance prosecution, applicant has amended the independent claims to recite "to alter contractile patterns and to prevent arrhythmias," which the Examiner acknowledges is supported by the specification.

The Examiner stated that claims 1, 9-11, 20, 28-30, 39 and 47-49 stand rejected under 35 U.S.C. 102(e) as being allegedly anticipated by Ben-Haim et al. (US 6363279) for the reasons of record.

The Examiner stated that Ben-Haim et al. teach a method of modifying the force of contraction of a heart by applying a non-excitatory electrical field. The Examiner stated that mechanical activation of the heart is controlled by electrical stimulation where action potentials from the S-A node enter the heart conduction system and propagate through the ventricles of the heart by sequentially activating connected muscle fibers (col. 1 @ 31-45). The Examiner stated that his invention focuses on controlling the heart by modifying the action potentials, the ionic pumps and the channels of the

heart (col. 2 @ 6 - col. 3 @ 32).

The Examiner stated that this invention focuses on controlling the heart by modifying the channels that connect the heart; the channels are read to include gap junction channels (col. 2 @ 6 - col. 3 @ 32). According the Ben-Haim et al., the Examiner stated, these channels of the heart are modified by electrical stimulation (col. 27 @ 12-27; col. 27 @ 52-57; col. 31 @ 1-5). The Examiner stated that, while Ben-Haim addresses the controlling the channels of the heart, the gap junction channels are not specifically mentioned. The Examiner stated that it is, however, inherent that the Ben-Haim et al. invention controls the gap junction channels as they are an essential component of the heart conduction system as noted in the art made of record (Winslow et al. US 5947899, - col. 5 @ 28 - col. 6 @ 3; col. 6 @ 33-53.

The Examiner stated that refractory periods are modified by electrical stimulation (col. 8 @ 3-5; col. 47 @ 37-45; col. 8 @ 66 - col. 9 @ 3; col. 9 @ 15-19; col. 17 @ 26-35; col. 17 @ 45-46; col. 31 @ 26-31).

The Examiner stated that ion channels are modified by electrical stimulation (col. 26@ 62-col. 27 @ 27; col. 27 @ 43-57; col. 31 @ 1-5).

The Examiner stated that changes in the heart occur over time as the heart is remodeled (col. 9 @ 51-55; col. 38 @ 48 - col. 39 @ 10). The Examiner stated that electrodes can be attached by sewing (col. 30 @ 9-12). The Examiner stated that electrodes can be placed in the heart or in vessels (col. 37 @ 30-35; col. 40 @ 48-51). The Examiner stated that electrodes

can be activated in pairs (col. 37 @ 15-17).

As to preventing arrhythmias, the Examiner stated that Ben Haim et al. disclose providing therapy to reduce the probability of ventricular fibrillation, read as preventing arrhythmias (col. 8 @ 44-48).

The Examiner stated that the applicant's arguments filed 4-18-03 have been fully considered, but they are not convincing.

The Examiner stated that the applicant appears to argue that the Examiner has misunderstood the meaning of the term "channels" used in Ben-Haim et al. (col. 2 @ 6-col. 3@ 32). The Examiner stated that the applicant appears to assert a definition for "channel" as used by Ben-Haim et al., but the applicant fails to provide citations from Ben Haim et al. to convince the Examiner that the applicant's interpretation of the term is correct. The Examiner stated that applicant states "transmembrane channels" are referred to as "ion channels" whereas the "gap junction" are referred to as "conneions", but the Examiner is unable to find this terminology in Ben Haim et al. The Examiner stated that lacking a convincing argument with citations, the rejections of record stand.

The Examiner stated that applicant argues the instant invention provides long-term remodeling and altering of the cardiac processes and Ben-Haim et al. only provides change and control of the cardiac processes in a current moment. The Examiner stated that applicant further asserts the Ben-Haim et al. method produces cardiac change only when the electrical stimulation is applied and the effect of the change ceases

when electrical stimulation ceases. The Examiner stated that he disagrees. The Examiner stated that Ben-Haim et al. does apply stimulation to create cardiac process changes in the current moment. The Examiner stated that in addition, Ben-Haim et al. recognize applying electrical stimulation in the current moment produces long-term/permanent changes of the cardiac processes, read as remodeling and altering of the cardiac processes. The Examiner stated that these long-term changes are reflected in a need for the therapy to be altered periodically and are reflected when treatment targets are met and the therapy is discontinued because the cardiac process has been changed to the point that therapy is no longer needed, hence Ben-Haim et al. disclose changes in the cardiac process in the moment and long-term (col. 9 @ 15-19; col. 9 @ 51 - col. 10 @3; col. 30 @ 34-37; col. 34 @ 15-38; col. 35 @ 55-59; col. 38 @ 48 - col. 39 @ 18).

The Examiner stated that applicant argues that since Ben-Haim et al. only changing the muscle mass of the heart over time, changing muscle mass does not necessarily result in remodeling the gap junction, altering the refractory period in the heart or inducing the ion channel remodeling.

The Examiner stated that he disagrees. The Examiner stated that Ben-Haim et al. disclose methods to control and change the electrical and mechanic activity of the cardiac muscle cells that produce changes the muscle mass and changes in the action potential plateau duration, the activation time, the activation sequence, the contractability and the conduction pathways of the cardiac segment, hence Ben-Haim is read to remodel gap junctions, alter the heart refractory period and induce ion channel remodeling (col. 2 @ 6-col. 3 @ 32; col. 7

@ 65-67; col. 34 @ 28-34).

The Examiner rejected Claims 2, 5, 12, 13, 15, 21, 24, 31, 32, 34, 40, 43, 50, 51, 53 and 58-60 under 35 U.S.C. 103(a0 as being allegedly unpatentable over Ben-Haim et al. (US 6363279) in view of Edwards et al. (US 5681308) for the reasons of record.

The Examiner stated that Ben Haim et al. disclose the claimed invention except for the 7cm x 1 cm (claims 4, 23 and 42) strip (claims 2, 13, 21, 32, 40 and 51) of electrode material having linked multiple electrode pairs, where the pairs ar arranged in two columns (12, 31 and 50) with one electrode in each pair in one column and the other electrode in each pair in the other column (claims 5, 15, 24, 34, 43, 53 and 58-60).

The Examiner stated that Edwards et al. disclose an analogous mapping apparatus and teach that it is known to use a circuit (38) mounted on a membrane support (16) to serve as a cardiac electrode which provides columns of individually controlled treatment electrodes (34) which can be multiplexed to enable stimulation of electrode pairs (figure 7; col. 7 @ 38-52). The Examiner stated that absent any teaching of criticality or unexpected results, it is understood the electrode can be configured as a 7cm x 1 cm strip with only two columns of electrodes. The Examiner stated that the configuration change is an obvious change in shape based on the specific application. The Examiner stated that, therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method for modifying the force of contraction of a heart as taught by Ben-aim et al., with the electrode as taught by Edwards et al.

to provide a flat electrode with multiple electrode measurement and stimulation configurations so the cardiac tissue can be more effectively treated.

The Examiner stated that Claims 3, 4, 14, 17-19, 22, 23, 33, 36-38, 41, 42, 52 and 55-57 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Ben-Haim et al. (US 6363279) in view of Edwards et al. (5681308) and further in view of Dahl et al. (US 5203348) for the reasons of record. The Examiner stated that, modified Ben-Haim et al. disclose the claimed invention except for:

- the electrode strip of polyurethane (claims 3, 14, 22, 33, 41 and 52),
- the electrode comprised of platinum or consisting essentially of unalloyed platinum (claims 17-18, 36-37 and 55-56), and
- the electrode connected to insulated stainless steel wire (claims 19, 38 and 57).

The Examiner stated that Dahl et al. disclose an electrode and teach that it is known to fabricate an electrode with a platinum or platinum alloy conductor or donductor with a stainless steel core (col. 4 @ 19-36), and alead with a medical grade polyurethane sheath and a stainless steel coated conductor (col. 5 @ 23-38). The Examiner stated that, therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the modified method for modifying the force of contraction of a heart as taught by Ben-Haim et al., with the materials of construction as taught by Dahl et al.. The Examiner stated that one having ordinary skill in the art would have been motivated to make such a modification in electrode to specify

materials of construction that have proven electrical properties.

The Examiner stated that claims 7, 8, 26, 27, 45 and 46 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Ben-Haim et al. (US 6363279) in view of Dahl et al. (US 5203348) for the reasons of record.

The Examiner stated that Ben-Haim et al. disclose the claimed invention except for the electrode being platinum or consisting essentially of unalloyed platinum.

The Examiner stated that Dahl et al. disclose an electrode and teach that it is known to fabricate an electrode with a platinum or platinum alloy conductor (col. 5 @ 23-38). The Examiner stated that, therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method for modifying the force of contraction of a heart as taught by Ben-Haim et al., with the platinum of platinum alloy conductor as taught by Dahl et al. The Examiner stated that one having ordinary skill in the art would have been motivated to make such a modification in electrode to specify materials of construction that have proven electrical properties.

The Examiner stated that claims 6, 16, 25, 35, 44 and 54 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Ben-Haim et al. (US 6363279) in view of Edwards et al. (US 5681308) and further in view of Ideker (US 5873896) for the reasons of record.

The Examiner stated that modified Ben-Haim et al. disclose the claimed invention except for the electrode pair being 2mm from each other and the electrode pairs being spaced at least 5mm apart.

The Examiner stated that Idecker teaches a cardiac device for reducing arrhythmias and teaches that it is known to use an electrode configuration of an elongate primary strip with a plurality of electrodes positioned at spaced intervals, e.g. 1-4 millimeters (col. 3 @ 2-4). The Examiner stated that therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the modified method for modifying the force of contraction of a heart as taught by Ben-Haim et al., with the electrode spacing as taught by Ideker to provide electrode spacing known to effectively reduce cardiac arrhythimias.

The Examiner stated that on page 40, line 23, it appears "duraction" should be -duration--. The specification is being amended to correct this spelling.

The Examiner stated that the Katz reference associated with the information disclosure statement (IDS) filed 4-18-03 fails to comply with 37 CFR 1.198(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Applicant submits herewith a copy of the Katz article, and a PTO-1449 form listing this reference.

The Examiner stated that in the listing of the claims in the Amendment filed 4-18-03, claim 43 is not the claim 43 of

record. The Examiner stated that it appears claim 39 was inadvertently duplicated and labeled as claim 43. The Examiner stated that claims 43 is noted to be "currently amended" however the Examiner believes this si a mistake and the rejection in the previous paragraphs of this action reflects claim 39 not being amended. The examiner stated that clarification and amendment of claim 39 to reflect the "pre-4-18-03" claim 39 appears to be needed. The Examiner stated that correction is required. Applicant has replaced claim 43 with the originally filed claim 43.

Applicant will address the rejections based on the Ben-Haim et al. U.S. Patent No. 6,363,279 particularly those rejections of anticipation of independent method claims 1, 20 and 39. The Ben-Haim reference relates to a device which applies an electrical field to the heart. Ben-Haim et al. state that their device modified the plateau currents, resulting what is claimed to be an increase in force of contraction. However, this reference does not contain any teaching or disclosure, explicitly or inherently, for causing the heart to be excited and activated, resulting in remodeling gap junctions, inducing ion channel remodeling or altering the effective refractory period to prevent or reverse arrhythmias.

The Examiner has cited column 2, line 6-column 3, and lines 32 of the Ben-Haim reference to allegedly show that Ben-Haim modifies the action potential, ionic pumps and channels of the heart. The Examiner further states that the "channels" are read to include "gap junction channels."

Applicant respectfully disagrees with the Examiner's statement that "channels" include "gap junction channels" or "gap

gap junction channels," but does not state that the Ben-Haim reference teaches remodeling gap junctions. As stated above Ben-Haim does not disclose remodeling gap junctions either expressly or inherently. Claims 1 and 12 recite that gap junctions are remodeled thus distinguishing them over Ben Haim. Accordingly, applicant believes that claims 1 and 12 are patentable over Ben-Haim.

The Examiner also stated that changes in the heart occur over time as the heart is remodeled and cites the Ben-Haim reference in column 9, lines 51-55 and column 38, line 48-column 39, line 10. These pages only state that by using electrical fields, one can change the muscle mass of the heart over time. However, changes to the muscle mass do not inherently or necessarily result in remodeling gap junctions, altering the refractory period in the heart, or inducing ion channel remodeling. Claims 20, 31, and 59 recite that the refractory period is altered, and claims 39, 50, and 60 recite that the ion channel is remodeled. None of this is taught by or inherently results from Ben-Haim.

The Examiner further stated that in Ben-Haim refractory periods and ion channels are modified by electrical stimulation. Ben-Haim, however, never discloses explicitly or inherently that ion channels remodeling is induced, or that refractory periods are altered by his electrical stimulation. While Ben-Haim in col. 26, line 62 et seq. mentions that electrical stimulation can change the movement of ion channels, such effect occurs only when the external electrical stimulation continues to be applied, but the effect ceases when the external electrical stimulation ceases. In contrast, applicant's claims 39, 50, and 60 recite that the ion channels

junctions." An ion channel merely connects the interior of a cell to the exterior of the same cell. A gap junction is not an ion channel, but is a specialized connection that connects the interior of one cell to the interior of another cell. The transmembrane channels are referred to as ion channels, whereas the gap junctions are referred to as connexions. When Ben-Haim uses the term channels, he is not referring to gap junctions, but instead is referring to voltage gate channels. The Ben-Haim reference does not explicitly disclose any remodeling of gap junctions.

In response to the Examiner's contention that "ion channels", as the term is used in Ben-Haim, includes "gap junctions", applicant submits an abstract of an article entitled Ion Channels and Gap Junctions: Their Role in Erectile Physiology, Sysfunction, and Future Therapy. Christ G.J. et al. Mol Urol 1999; (3(2): 61-73 (Abstract only) which abstract uses these terms in a mutually exclusive way to refer to different things. Accordingly, one skilled in the art as of applicant's filing date would not interpret "ion channels" to include "gap junctions".

Furthermore, Ben-Haim does not inherently remodel gap junctions. If one skilled in the art followed the disclosure and direction provided by Ben-Haim to change the ion channels, this change could be done without also remodeling the gap junctions. Accordingly, Ben-Haim does not <u>inherently</u> remodel gap junctions because modification of gap junctions would not necessarily occur when following the Ben-Haim disclosure to change ion channels.

The Examiner stated that "the Ben-Haim invention <u>controls</u> the

gap junction channels," but does not state that the Ben-Haim reference teaches remodeling gap junctions. As stated above Ben-Haim does not disclose remodeling gap junctions either expressly or inherently. Claims 1 and 12 recite that gap junctions are remodeled thus distinguishing them over Ben Haim. Accordingly, applicant believes that claims 1 and 12 are patentable over Ben-Haim.

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are remodeled, such that when electrical stimulation is applied, the ion channels are remodeled and remain in their remodeled state even after external electrical stimulation is removed.

Similarly, claims 20, 31 and 59 recite that the refractory period is altered, and remains altered after external electrical stimulation is removed. In Ben-Haim, any change in refractory period is lost when the external electrical stimulation is removed.

The presently claimed invention of claims 1, 20 and 39 provides an electrical stimulus to the heart that excites the heart and results in altered activation, which must occur for the downstream changes to occur in remodeling gap junction, inducing ion channel remodeling or altering the effective refractory period. While the objective of the Ben-Haim et al. device is to improve cardiac failure, the methods of the presently claimed invention are to prevent arrhythmias of many causes (by remodeling gap junctions, inducing ion channel remodeling or altering the effective refractory period), not just causes associated with congestive failure. For the foregoing reasons, applicant urges that Ben-Haim et al. fail to disclose, explicitly or inherently, the methods of claims 1, 20 and 39.

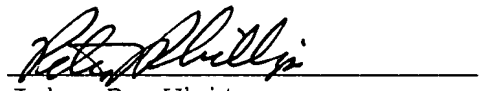
The other rejections are based on the Ben-Haim et al. reference in combination with at least one other reference, and rely on the Ben-Haim et al. reference as a primary reference. However, as discussed above, the Ben-Haim et al. reference fails to teach or suggest any aspect of remodeling

gap junctions, altering the refractory period in the heart, or inducing ion channel remodeling to prevent arrhythmias. The other references also fail to remedy the deficiencies of Ben-Haim in this respect. Therefore, these proposed combinations necessarily fail to teach or suggest the claims against which they were cited. Moreover, applicant urges that there is no teaching or suggestion in the prior art or otherwise of anything that would motivate one of ordinary skill in the art to combine the references as proposed by the Examiner.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone them at the number provided below.

Applicant submits the fee of $180 under 37 C.F.R. § 1.17(p) for consideration of the Katz reference. No other fee is deemed necessary in connection with the filing of this Response. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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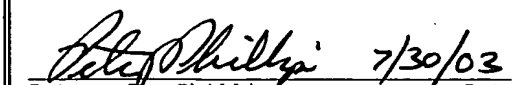

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